SEAMO Innovation Showcase 2018

Taking a peek under the hood: Non-invasive assessments of brain function in critically ill patients

J. Gordon Boyd, MD, PhD SEAMO Clinician-Scientist

Associate Professor Depts of Medicine (Neurology) and Critical Care Medicine

## How is the heart monitored in critically ill patients?



## How is the brain monitored in critically ill patients?



## How is the brain monitored in critically ill patients?

The clinical neurological exam is limited in critically ill patients:

-Severity of illness -Sedative medications -Analgesic medications Research program beginnings:

## Can we identify novel biomarkers of brain injury in critically ill patients?

SEAMO Innovation Fund 2014 Small pilot/feasibility study

Serum proteomics to identify novel biomarkers of brain injury after cardiac arrest



11 patients recruited after cardiac arrest Blood collected every 12h for 3 days Serum proteome separated with 2D gel electrophoresis Protein differences between good outcome patients and poor outcome patients identified with mass spectrometry

### CrossMark

### Serum proteomics as a strategy to identify novel biomarkers of neurologic recovery after cardiac arrest: a feasibility study

J. Gordon Boyd<sup>1,2,4\*</sup>, Laura J. Smithson<sup>2</sup>, Daniel Howes<sup>1</sup>, John Muscedere<sup>1</sup>, Michael D. Kawaja<sup>3</sup> and On behalf of the Canadian Critical Care Translational Biology Group

- A. Good neurological recovery (CPC1-2)
- B. Poor neurological recovery (CPC 4-5)



#### C. Protein identification

Spot number	Protein identification
1	protein AMBP
2	Coiled-coil domain-containing protein 71
3	C-reactive protein
4	C-reactive protein
5	Retinol binding protein 4
6	Retinol binding protein 4
7	serum amyloid P component
8	serum amyloid P component
9	alpha beta hydrolase domain containing protein 14B
10	RRP15-like protein
11	40S ribosomal protein s24
12	Arf-GAP with GTPase ANK repeat and PH domain-containing protein 2
13	unidentified
14	14-3-3 epsilon
15	muskelin
16	14-3-3 zeta
17	Electrogenic sodium biicarbonate cotransporter 1
18	F151A

Next steps: Multi-centre study (LHSC, UBC, KHSC) with novel proteomics techniques (Innovation Fund 2016)

### Non-invasive strategies to measure brain function: Electroencephalography (EEG)

#### Advantages:

- -non-invasive
- -can detect non-convulsive seizures-portable

Disadvantages:

- -time consuming
- -labour intensive

-requires considerable expertise in interpretation, which may lead to delays in reporting EEG utilization in Canadian intensive care units: A multicentre prospective observational study

Andrea Park<sup>a</sup>, Martin Chapman<sup>b</sup>, Victoria A. McCredie<sup>b</sup>, Derek Debicki<sup>c</sup>, Teneille Gofton<sup>c</sup>, Loretta Norton<sup>c</sup>, J. Gordon Boyd<sup>a,d,\*</sup>



EEG is only performed in 37% of indicated cases

### Other non-invasive strategies to measure brain function: Near-infrared spectroscopy (NIRS)

Measuring regional cerebral oxygenation  $(rSO_2)$  with NIRS has been studied for over a decade in the cardiac OR

Lower levels of rSO<sub>2</sub> are correlated with increased likelihood of developing cognitive dysfunction after cardiac surgery.



HYPOTHESIS: Do low levels of cerebral oxygenation correlate with acute neurological dysfunction (i.e. delirium) in critically ill patients?

## Methods:

Enrolled patients at KHSC in respiratory failure or shock

Recorded rSO2 for first 72 hours of critical illness

Assessed for acute neurological dysfunction (i.e. delirium) daily until ICU discharge

Delirium was chosen as outcome measure, since:

-independent risk factor for ICU mortality and LOS -most consistent risk factor for long-term cognitive impairment among ICU survivors



Shown with permission

## Low brain tissue oxygenation contributes to the development of delirium in critically ill patients: A prospective observational study



The Cerebral Oxygenation and Neurological Outcomes Following Critical Illness (CONFOCAL) Research Group, on behalf of the Canadian Critical Care Trials Group. Michael D. Wood, BA<sup>a,1</sup>, David M. Maslove, MSc, MD<sup>b,c,2</sup>, John G. Muscedere, MD<sup>b,3</sup>, Andrew G. Day, MSc<sup>d</sup>, J. Gordon Boyd, MD, PhD<sup>a,b,c,\*,4</sup>

Mean cerebral oxygenation was lower in patients who spent the majority of their ICU stay delirious

Together with higher fentanyl use and history of alcohol abuse, low cerebral oxygenation was an independent risk factor for the development of delirium

Considerable variability within groups however



#### NIH U.S. National Library of Medicine

#### ClinicalTrials.gov

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Cerebral Oxygenation and Neurological Outcomes FOllowing CriticAL Illness-2 (CONFOCAL-2)

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ClinicalTrials.gov Identifier: NCT03141619

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Recruitment Status : Recruiting First Posted : May 5, 2017 Last Update Posted : March 2, 2018

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Next steps: Explore further in multi-centre study

PSI New investigator award 2016

# Summary

\* The brain is no longer a "black box" in the ICU, and non-invasive tools exist that may provide assessments of function to supplement the clinical exam

 One may envision a future where these tools are used to guide therapy, in order to improve neurological outcomes after critical illness

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